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On June 10, 2005

TOWNSEND and TOWNSEND and CREW LLP

By: [Signature]

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

EISENBERG et al.

Application No.: 09/825,242

Filed: April 2, 2001

For: SELECTION OF SITES FOR
TARGETING BY ZINC FINGER
PROTEINS AND METHODS OF
DESIGNING ZINC FINGER PROTEINS
TO BIND TO PRESELECTED SITES

Examiner: John Brusca

Art Unit: 1631

REPLY BRIEF

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Sir:

In response to the Answer mailed April 19, 2005, appellants submit the attached Reply Brief.

REPLY BRIEF

The Appeal Brief pointed out that the cited references do not disclose a database comprising designations for a plurality of three-finger zinc finger proteins, subdesignations for each of three fingers for each zinc finger protein, and their corresponding target nucleic acid sequences, as specified in claim 35, 40, 48, 49 and 53. The references cited by the Examiner for disclosure of a database, namely Choo 1994(b) and Choo 1994(a) suffer from the same deficiency in that both provide designations for only a single finger of a multi-finger zinc finger protein and neither presents a target sequence with three triplets. Because the combination of references does not teach a database comprising designations of multi-finger zinc finger proteins and subdesignations of each of three fingers for each zinc finger protein, it follows that the combination of reference sequences also does not disclose step (c) of the above claims of identifying first, second and thirds sets of zinc finger proteins in the database. Similarly, the combination of references does not teach step (d) of the above claims of outputting designations and subdesignations of the zinc finger proteins.

Appellants have also pointed to a lack of motivation to combine Corbi with Choo (1994a). The zinc finger components of Corbi's zinc finger protein would not bind to the triplets of Choo (1994b), and would be of no apparent use in Choo (1994b)'s goal of designing a zinc finger protein to bind to the Bcr-Abl target.

The Examiner's comments in section (9) of the Answer "Grounds of Rejection" appear to be identical to the rejection in the final office action of October 7, 2004, which was addressed in the Appeal Brief. Accordingly, no further response is necessary.

In section (10) of the Answer, the Examiner addresses some but not all of appellants' remarks in the Appeal Brief. First, the Examiner alleges that Choo (1994a) does disclose a database of three-finger zinc finger proteins in that table 2 of the reference represents fingers that were selected as components of three-finger zinc finger proteins (Answer at p. 6). However, the Examiner has not addressed the substance of appellants' position that although the physical zinc finger proteins, from which the

information described in the cited references was obtained, may inherently have had three zinc fingers, these physical proteins are not components of a database.

Next the Examiner states "The applicants state on page 8 that the library members detailed in Choo et al. (1994a) are not the members selected by Choo et al., (1994b), however, the combination of references shows a large precharacterized library of 2,600,000 members on p. 11164, second column that are characterized as to binding specificity to a wide range of target nucleotide triplets in Figure 2." Again, this remark misses the substance of appellants' position (appeal brief at p. 8, first full paragraph). The advisory action's proposal to modify the teaching of the secondary reference Choo (1994a) for some purpose unrelated to the primary reference Choo (1994b) would not have suggested modification of the primary reference. Appellants also note that the library of 2,600,000 referred to by the Examiner is a library of physical phage particles rather than a database. Moreover, the teaching of a library of 2,600,00 phage is that of Choo et al. (1994b) alone, not the combined teaching of the references.

Next the Examiner states that Choo (1994b) further characterized the library of Choo (1994a) to detect desired binding specificities for the purpose of designing three finger zinc finger proteins, as recited in the claims (Answer at p. 7). Although the ultimate goal of Choo (1994b) may have been to produce a three-finger zinc finger protein, such as specified in the final step of claim 35, what is at issue is not the final product of the present claims, but rather the combination of method steps recited in the present claims. As summarized above, the combination of methods steps is not disclosed or suggested by the cited references.

Next the Examiner alleges that Choo (1994a) does provide guidance regarding zinc finger proteins, citing to the last sentence on p. 11163. However, p. 11163, second column, first paragraph explains that the design process referred to is one using rules that relate amino acids in a zinc finger protein to corresponding bases in a bound DNA sequence. This is distinct from the database approach of the presently claimed methods in which no such rules are necessary. It is unclear how the sentence cited by the Examiner is relevant to the claimed methods or to any basis of rejection.

Next, the Examiner repeats his argument from the advisory action that it would have been obvious to include the zinc finger protein of Corbi in the database of Choo (1994b) [the secondary reference] to make the database as large as possible and to allow for selection of zinc fingers of any desired specificity. The Examiner has not addressed appellants' response thereto that the alleged database of Choo (1994a) summarizes results from a particular experiment, and it would not be usual scientific practice to merge data from a particular experiment with data from any and all known zinc finger proteins regardless of how the data were obtained. The Examiner has also not addressed appellants' further point that Choo (1994a) is cited as a secondary reference to modify the teachings of Choo (1994b). Even if it is assumed *arguendo* one might want to modify Fig. 2 of Choo (1994a) to include data from additional zinc finger proteins albeit for a purpose not specified in the reference, this does not mean one would want similarly to modify the "database" of Choo (1994b) to include Corbi's protein. Finally, the alleged motivation to make the "database" of Choo et al. (1994b) as large as possible to select for zinc fingers of any desired specificity (Examiner's Answer, page 7), is present in neither the references themselves nor in the art as a whole, inasmuch as Choo et al. (1994b) successfully obtained zinc finger proteins capable of regulating their target gene and thus had no need to seek or design additional zinc finger proteins.

Finally, the Examiner repeats his position from the advisory action that the large size of the zinc finger library makes complete characterization impractical without computer-mediated entry and search capabilities of the associated database. However, the Examiner has not addressed appellants' response in the appeal brief. Even if it is assumed *arguendo* that it were obvious to use a computer to analyze the data of Choo (1994a) for some purpose such as data storage or search (albeit not disclosed in the reference) this does not mean that it would have been obvious to use a computer to automate the design of a protein from the data in Fig. 2 of Choo (1994b) according to the specific steps of claims 48, 49 and 53.

For these reasons, as well as those submitted in the Appeal Brief, it is respectfully submitted the rejection should be reversed.

Respectfully submitted,

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